Dear Editors and Reviewers:

Thank you very much for your letter and for the reviewers' comments concerning our manuscript entitled "Prediction of microvascular invasion in solitary hepatocellular carcinoma ≤5 cm based on CT radiomics". Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our research. We have studied comments carefully. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as following:

Reviewer 1

1. By retrospective analysis and validation control, the study showed that CT radiomics has a certain predictive value in MVI in solitary HCC ≤5 cm, compared to imaging features (TTPVI and RVI). It is significance for surgery choice in patients with HCC. But I think that there is not enough for only two radiologic features (Reference: Radiomic analysis of contrast-enhanced CT predicts microvascular invasion and outcome in hepatocellular carcinoma).

Response: Thanks for reviewer's guidance. First, these two radiologic features (i.e. RVI and TTPVI) we evaluated were based on two published seminal studies, which suggested RVI and TTPVI were promising and reliable biomarkers to preoperatively predict MVI [1,2].

Second, some features in the provided Reference (Radiomic analysis of contrast-enhanced CT predicts microvascular invasion and outcome in hepatocellular carcinoma), such as number of lesions, maximum tumor length, lobes with tumor involvement, are not applicable for our study, because we focused on the patients with solitary hepatocellular carcinoma ≤5 and most of the tumors involved only 1 lobe. Besides the patients with peritumoral star lesion was excluded in our study.

Third, compared with RVI or TTPVI, these features (as evaluated in the provided reference) including tumor margin, growth pattern, capsule, peritumoral enhance have not yet been widely recognized. However, we have to acknowledge that they may have higher association of MVI but were not evaluated in this study, just as you pointed out. The value of these features will be explored and validated in the future study.

[1] Renzulli M, Brocchi S, Cucchetti A, et al. Can Current Preoperative Imaging Be Used to Detect Microvascular Invasion of Hepatocellular Carcinoma. Radiology. 2016. 279(2): 432-442.

[2] Banerjee S, Wang DS, Kim HJ, et al. A computed tomography radiogenomic biomarker predicts microvascular invasion and clinical outcomes in hepatocellular carcinoma. Hepatology. 2015. 62(3): 792-800.

2. Why focused on the solitary hepatocellular carcinoma ≤5?

Response: Thanks for reviewer's question. According to Hong Kong Liver Cancer staging system, Early tumor had a size of ≤5 cm and no intrahepatic venous Invasion

[1], This kind of tumor had significant improved survival benefit of radical therapies. Therefore, accurately identifying MVI before surgery was more important. Our research subjects are Chinese. Unlike other countries, the cause of liver cancer is mostly hepatitis B infection. So, we adopted Chinese standards and selected this kind of patients.

[1] Yau Thomas,Tang Vikki Y F,Yao Tzy-Jyun et al. Development of Hong Kong Liver Cancer staging system with treatment stratification for patients with hepatocellular carcinoma.[J] .Gastroenterology, 2014, 146: 1691-700.e3.
[2] Wang Han,Yu Hua,Qian You-Wen et al. Impact of Surgical Margin on the Prognosis of Early Hepatocellular Carcinoma (≤5 cm): A Propensity Score Matching Analysis.[J] .Front Med (Lausanne), 2020, 7: 139.

3. In the section of introduction，the sentence"At present, few studies have focused on the prediction of MVI in the early stage of HCC (which refers to solitary and a tumor size of ≤5 cm, without MVI)."，which has no evidence（including reference） to support. Please give references or other evidence.

Response: Thanks for reviewer's kind suggestion. We added the reference [1]Yau Thomas,Tang Vikki Y F,Yao Tzy-Jyun et al. Development of Hong Kong Liver Cancer staging system with treatment stratification for patients with hepatocellular carcinoma.[J] .Gastroenterology, 2014, 146: 1691-700.e3.
[2] Chong Huan-Huan,Yang Li,Sheng Ruo-Fan et al. Multi-scale and multi-parametric radiomics of gadoxetate disodium-enhanced MRI predicts microvascular invasion and outcome in patients with solitary hepatocellular carcinoma≤5 cm.[J] .Eur Radiol, 2021, undefined: undefined.

4. In the section of "Examination methods", "The images at the arterial phase, portal phase, or delayed phase were obtained at 30, 60 and 120 seconds after the injection of the contrast agent", the delayed time for three phases is optimal?

Response: Thanks for reviewer's question. That is an average number. Actually, dynamic contrast-enhanced imaging data acquisition was performed at fixed time points: for the arterial phase, acquisition occurred at approximately 25–33 s after administration; for the portal vein phase, it was 57–63 s, and for the delayed phase, 117–123s. In order to make the expression more rigorous, we revised the above sentence.

5. The title of Fig4 doesn't make sense.

Response: Thanks for reviewer's kind suggestion. Do you mean that Fig4 is duplicated with Table2, should Fig4 be deleted? We also agree to delete Fig4, which is represented by Table 2.

6. Tn the third paragraph of discussion, what is the "The Norman model？"or spelling mistake?

Response: Very sorry for this spelling mistake. It should be nomogram.

Reviewer 2

1. The authors described the inclusion and exclusion criteria. The collected patients were selected consecutively? According to the Table 1, the tumor sizes were 36(28:44), 34(27.5:41) in each group. Is there anyone less than those sizes in this period? MVI is more frequent present and more easily detected in radiomics in bigger tumor. So, the details of the tumor size should be included.
Response: Thanks for reviewer's kind suggestion. Yes, the collected patients were selected consecutively. The details of the tumor size had been included in the article. The study consisted of 185 patients. Tumor size ranged from 10mm to 50mm.

2. Inclusion criteria: (1) .... ; (2) tumor with the maximum diameter of <5 cm. ----> 'less than 5 cm', 'solitary HCC ≤5 cm' should be unified.
Response: Thanks for reviewer's kind reminder. We unified the data.

3. The authors described the limitations of this study - retrospective and single-center study, study only used arterial phase images. However, this study raise the value of the radiomics model in HCC very much.
Response: Thanks for reviewer's evaluation. Our study found that CT radiomics has certain predictive value for MVI in solitary HCC≤5cm. However, it is still an exploratory study since the sample size and single-center data. Before it is applied to clinical practice, further big data and multi-center research are still needed.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper.

We appreciate for Editors/Reviewers' warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.